PATENT
Previous Atty Docket No. 071949-1307
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application:		Confirmation No.:	**9972**
Inventor:	Kenneth F. Buechler	Examiner:	Alexander, Lyle
Application No.:	09/613,650	Group Art Unit:	1743
Filed:	7/11/2000	Customer No.	**21971**
Title:	DIAGNOSTIC DEVICES AND APPARATUS FOR THE CONTROLLED MOVEMENT OF REAGENTS WITHOUT MEMBRANES		

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APPEAL BRIEF

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Sir:

Applicant (hereinafter "Appellant") hereby appeals the Final Rejection of claims 74-84 and 92-100. This Appeal Brief follows a Notice of Appeal filed January 8, 2008 The fee for this Appeal Brief (37 C.F.R. § 41.20(b)(2)) accompanies this filing. If the fee is absent or incorrect or if any additional fees are due in this regard, please charge or credit our Deposit Account No. **23-2415** (Docket No. 36671-716.505) for the appropriate amount.

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FEDERAL CASES

Real Party in Interest

The real party in interest in this appeal is Biosite Incorporated, which is the assignee of the present application.

Related Appeals and Interferences

The present application was the subject of an Appeal Brief filed on January 22, 2007. Following submission of that Appeal Brief, the Examiner reopened prosecution of the application in an Office Action mailed July 13, 2007. In accordance with MPEP §1207.04, Appellant has initiated the present appeal by filing a notice of appeal under 37 CFR41.31, followed by submission of the present Appeal Brief under 37 CFR 41.37.

U.S. Patent Applications 10/153,423 and 10/697,351, each of which is presently on appeal, relates to the present application in so far as the claims relate to devices for handling of fluid samples, are also assigned to Biosite Incorporated, and have been examined by the same Examiner as the present application.

Status of Claims

Claims 1-73 and 85-91 have been cancelled.

Claims 74-84 and 92-100 are pending in the application. For the convenience of the Board, the pending claims are presented in Appendix A of this Brief.

Claims 74-84 and 92-100 are the subject of this appeal.

Claims 74-84 and 92-100 stand rejected under the judicially created doctrine of obviousness-type double patenting over U.S. Patent 5,458,852.

Claims 74-81 and 92-100 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Claims 74-81 and 92-99 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly failing to comply with the definiteness requirement.

Claims 74-81 and 92-99 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Stöcker, U.S. Patent 4,647,543.

Claims 82 and 100 stand finally rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Stöcker, U.S. Patent 4,647,543, either alone or in view of Anawis and Lingberg, U.S. Patent 5,091,318, or Rohr, U.S. Patent 5,445,970.

Status of Amendments

In response to the obviousness-type double patenting rejection over U.S. Patent 5,458,852, a terminal disclaimer was submitted by Appellant on November 30, 2006. Despite this fact, the Examiner has not addressed Appellant's submission, and has maintained the obviousness-type double patenting rejection over the '852 patent. Appellant respectfully submits that this submission renders moot the rejection of claims 74-84 and 92-100 under the judicially created doctrine of obviousness-type double patenting.

As this is the only rejection pending for claims 83 and 84, Appellant believes that these claims are in condition for allowance following submission of the terminal disclaimer.

No other amendments or submissions are pending in the application.

Summary of Claimed Subject Matter

The claimed subject matter relates in part to assay devices for measuring analytes of interest ("target ligands") in fluid samples. In particular, the present invention provides device components that provide for controlled movement of fluids in various regions of such devices.

Numerous test devices and systems that employ such devices have been developed over the years for measuring the presence or concentration of analytes in fluid samples, such as whole blood or urine. As discussed in some detail on pages 1 and 2 of the present specification, these devices typically employed test reagents and some sort of absorbent member through which the fluid sample flows. Typical absorbent members include paper materials, glass fiber mats, porous membranes, etc., which move fluids by capillary action. Specification, page 1, line 28, through page 2, line 24. Devices that rely on such porous materials can suffer from problems with

consistency of capillary flow and binding characteristics from device batch to device batch. This is often because production of these porous materials is not easily reproducible in terms of their microscopic and macroscopic features. Specification, page 5, lines 3-12. In addition, devices previously known in the art often require precise delivery of fluids and careful handling of reagents, and so must be used by relatively skilled users in a laboratory setting. Specification, page 2, lines 25-28.

To avoid such issues, the present invention relates to assay devices that rely on one or more nonporous surfaces having defined surface characteristics to regulate fluid flow. By carefully controlling the surface characteristics of the nonporous surface used, the present invention provides devices that do not require precise fluid handling or carefully timed incubations. Instead, the device may be used in a "fill-and-forget" fashion, in which the characteristics of the surface provide for regulated fluid flow. Specification, page 5, line 3, through page 6, line 6. One method for directing flow through specific regions of the device, and in particular for directing materials only to certain areas of a "diagnostic element" that captures target ligands for detection, involves delimiting certain regions of an otherwise hydrophilic surface with hydrophobic materials. Specification, page 27, line 31, through page 28, line 7. Arranging the device surface in this manner preferentially directs fluid flow to desired areas of the device, as fluid will tend to remain in the areas that are hydrophilic, and be repelled from areas that are hydrophobic.

Thus, the present invention claims assay devices for detecting a plurality of target ligands in a sample. As defined in independent claim 74, these devices comprise:

(a) a nonporous smooth surface or a nonporous textured surface; and

(b) a plurality of discrete capture zones on the surface, where each said capture zone comprises receptors immobilized to the surface or immobilized on particles immobilized to said surface, and where the receptors are capable of binding one or more of the plurality of target ligands being detected;

(c) wherein the capture zones occupy one or more discrete hydrophilic regions of said surface delimited by an adjacent hydrophobic region of said surface.

Further defining these devices, claim 74 also states (i) if the surface is the nonporous textured surface, the texture comprises one or more depressions or protrusions extending between 1 nm and 0.5 mm from the surface; and (ii) if the receptors are immobilized on particles, the particle size range is from 1 nm to 5 μm. Support for claim 74 is found in the application, for example at p. 5, lines 3-5; p. 7, lines 26-29; p. 15, lines 26-27; p. 17, lines 5-6; p.23, lines 24-27, p. 25, lines 1-19 and 22-29; p. 28, lines 11-16 and 21-24; and Figure 3.

In various dependent claims, the devices are further defined as comprising specific types of receptors (claims 75, 77, 78, and 80), as having discrete capture zones that each bind a different target ligand (claim 76), as comprising immobilized particles (claim 79), as comprising a textured surface, where the particles are entrapped within depressions in the surface (claim 81), as comprising specific types of particles (claim 82), as having a second surface that forms a capillary space with the nonporous surface (claim 83), and as not being part of a capillary space (claim 84).

Support for 75, 77, 78, and 80 is found in the application, for example at p. 9, lines 19-21; support for claim 76 is found in the application, for example at p. 25, lines 8-9; support for claim 79 is found in the application, for example at p. 25, lines 24-31; support for claim 81 is found in the application, for example at p. 28, lines 11-16; support for claim 82 is found in the application, for example at p. 25, lines 22-29; support for claim 83 is found in the application, for example at p. 5, lines 29-32; and support for claim 84 is found in the application, for example at p. 26, lines 15-21.

In independent claim 92, the claimed devices comprise an additional element not specifically recited in independent claim 74: that the capture zones are located in one or more diagnostic elements. Support for claim 92 is described in the specification, for example, at page 31, lines 16-19. Following this claim, the devices are further defined as comprising specific types of receptors (claims 93, 95, 96, and 98), as having discrete capture zones that each bind a different target ligand (claim 94), as comprising immobilized particles (claim 97), as comprising a textured surface, where the particles are entrapped within depressions in the surface (claim 99), and as comprising specific types of particles (claim 100).

Support for claims 93, 95, 96, and 98 is found in the application, for example at p. 9, lines 19-21; support for claim 94 is found in the application, for example at p. 25, lines 8-9; support for claim 97 is found in the application, for example at p. 25, lines 24-31; support for claim 99 is found in the application, for example at p. 28, lines 11-16; and support for claim 100 is found in the application, for example at p. 25, lines 22-29.

Grounds for Rejection to be Reviewed on Appeal

1. The rejection of claims 74-84 and 92-100 under the judicially created doctrine of obviousness-type double patenting over U.S. Patent 5,458,852.

2. The rejection of claims 74-81 and 92-100 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

3. The rejection of claims 74-81 and 92-99 under 35 U.S.C. §112, second paragraph, as allegedly failing to comply with the definiteness requirement.

4. The rejection of claims 74 and 92 under 35 U.S.C. §102(b), as allegedly being anticipated by Stöcker, U.S. Patent 4,647,543 (hereinafter "the '543 patent").

5. The rejection of claims 75 and 93 under 35 U.S.C. §102(b), as allegedly being anticipated by the '543 patent.

6. The rejection of claims 76 and 94 under 35 U.S.C. §102(b), as allegedly being anticipated by the '543 patent.

7. The rejection of claims 77 and 95 under 35 U.S.C. §102(b), as allegedly being anticipated by the '543 patent.

8. The rejection of claims 78 and 96 under 35 U.S.C. §102(b), as allegedly being anticipated by the '543 patent.

9. The rejection of claims 79 and 97 under 35 U.S.C. §102(b), as allegedly being anticipated by the '543 patent.

10. The rejection of claims 80 and 98 under 35 U.S.C. §102(b), as allegedly being anticipated by the '543 patent.

11. The rejection of claims 81 and 99 under 35 U.S.C. §102(b), as allegedly being anticipated by the '543 patent.

12. The rejection of claims 82 and 100 under 35 U.S.C. §103(a), as allegedly being unpatentable over the '543 patent, either alone or in view of Anawls et al., U.S. Patent 5,091,318 (hereinafter "the '318 patent"), or Rohr, U.S. Patent 5,445,970 (hereinafter "the '970 patent").

Argument

In the following remarks, Appellant will refer to the Examiner's statement of the various rejections made in the Office Action mailed on July 13, 2007. Hereinafter, this will be referred to as the "Office Action."

1. Rejection of claims 74-84 and 92-100 under the judicially created doctrine of obviousness-type double patenting over U.S. Patent 5,458,852

Appellant respectfully submits that the rejection of claims 74-84 and 92-100 has been overcome, and requests that the rejection be withdrawn or reversed.

The Examiner has maintained a rejection under the judicially created doctrine of obviousness-type double patenting over U.S. Patent 5,458,852. Office Action, page 2, final paragraph. In response to the obviousness-type double patenting rejection, however, a terminal disclaimer was submitted by Appellant on November 30, 2006. Appellant respectfully submits that this terminal disclaimer overcomes the rejection. See *In re Lonardo*, 119 F.3d 960, 965, 43 USPQ2d 1262, 1266 (Fed.Cir.1997) ("Obviousness-type double patenting ... is judicially created and prohibits an inventor from obtaining a second patent for claims that are not patentably distinct from the claims of the first patent. With obviousness-type double patenting ... a terminal disclaimer may overcome that basis for unpatentability, assuming that the first patent has not expired") (internal citations omitted).

In view of the foregoing, Appellant respectfully requests that the rejection of claims 74-84 and 92-100 be withdrawn or reversed.

2. Rejection of claims 74-81 and 92-100 under 35 U.S.C. §112, first paragraph (written description)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case that the present application fails to satisfy the written description standard of 35 U.S.C. §112, first paragraph. For these reasons, Appellant respectfully requests that the rejection of claims 74-81 and 92-100 be withdrawn or reversed.

The rejection contends that "[t]he original specification does not teach the claimed "nonporous surface." Office Action, page 3. Appellant respectfully submits that whether or not the claim limitation is literally present in the specification is not a proper standard for assessing compliance with the written description requirement. Rather than a requirement for *literal* support in the specification, the proper standard for determining compliance with the written description requirement is whether the specification reasonably conveys to the skilled artisan that the inventor was in possession of the claimed invention as of the filing date. *See, Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985). The present specification and claims meet this standard.

The present specification states on page 5, lines 3-24, that the devices described in the specification "do not use bibulous or porous materials, such as membranes and the like as substrates for the immobilization of reagents or to control the flow of the reagents through the device.... The devices of the current invention circumvent these membrane associated problems by the use of defined surfaces, including grooved surfaces, capillarity, time gates, novel capillary means, including channels and novel fluid flow control means alone or in various combinations, all of which are constructed from non-absorbent materials."

In view of this teaching, Appellant submits that the assertion that "[t]he original specification does not teach the claimed "nonporous surface." is without merit, and that the specification reasonably conveys to the skilled artisan that the inventor was in possession of the claimed invention as of the filing date. The written description standard demands no more

The Examiner's request that Appellant "[add] 'nonporous' to the instant specification" in order to overcome the rejection (Office Action, page 3) is unusual. The Examiner correctly notes that a parent of the present application, U.S. Patent 6,019,944, includes this same limitation in its issued claims. Office Action, page 3. Appellant notes that the support in the description of U.S. Patent 6,019,944 for the claim limitation is identical to that of the present specification. Moreover, the earliest document to which the present application claims priority, U.S. Patent 5,458,852, filed May 21, 1992, also contains the above-quoted language from the present specification in column 2, lines 4-7.

In view of the foregoing, Appellant respectfully submits that the claims meet the written description standard, and requests that the rejection of claims 74-81 and 92-100 be withdrawn or reversed.

3. Claims 74-81 and 92-99 under 35 U.S.C. §112, second paragraph, as allegedly failing to comply with the definiteness requirement

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case that the present application fails to satisfy the definiteness standard of 35 U.S.C. §112, second paragraph. For these reasons, Appellant respectfully requests that the rejection of claims 74-81 and 92-99 be withdrawn or reversed.

The rejection contends that "[t]he structure of independent claims 74 and 92 are confusing." Office Action, page 3, final paragraph. To the contrary, the meaning of these claims is plain.

The claims refer to the following structures:

a nonporous smooth surface or a nonporous textured surface, said nonporous textured surface comprising one or more depressions or protrusions extending between 1 nm and 0.5 mm from said nonporous textured surface; and

a plurality of discrete capture zones on said surface, each said capture zone comprising receptors immobilized to said surface or immobilized on particles immobilized to said surface, wherein said particle size range is from 1 nm to 5 μm, and wherein said receptors are capable of binding one or more of said plurality of target ligands,

> wherein said capture zones occupy one or more discrete hydrophilic regions of said surface delimited by an adjacent hydrophobic region of said surface

The Examiner states that "[t]he following permeation [sic] of the claimed subject matter is available for examination:

I) a nonporous smooth surface with receptor immobilized to the surface;

II) a nonporous smooth surface with receptor immobilized on particles immobilized to the surface;

III) a nonporous textured surface with receptor immobilized to the surface; and

IV) a nonporous textured surface with receptor immobilized on particles immobilized to the surface."

Office Action, page 4. Appellant agrees with the Examiner that the claims refer to these four possibilities.

The Examiner has not explained why the claim language might be so ambiguous as to defy understanding, and one is left to wonder what about this language might be "confusing" to the Examiner. The rejection is apparently not based on the proper standard by which definiteness is judged. The threshold for finding indefiniteness is very high:

> The threshold for indefiniteness is very high: the claim must be "insolubly ambiguous". . . . If one of skill in the art would understand the scope of the claim when read in light of the specification, then the claim complies with § 112(2). Claims need not be models of clarity. As long as the meaning is discernible, then even if construction is difficult and the result equivocal, the claim is nevertheless definite. Exxon Research & Eng'g Co., 265 F.3d at 1375, 60 USPQ2d at 1276; All Dental Prodx LLC v. Advantage Dental Prods., Inc., 309 F.3d 774, 779-80, 64 USPQ2d 1945, 1949 (Fed. Cir. 2002) (no indefiniteness despite the lack of clarity).

Scripps Research Institute v. Nemerson, 78 U.S.P.Q.2d 1019, 1030 (BPAI 2005). When judged by this standard, it is clear that the present claims are not "insolubly ambiguous," and so meet the definiteness standard.

The rejection also avers to claim 79, although it does not appear to be in the context of a rejection. As noted above, claim 74 refers to "a plurality of discrete capture zones on said surface, each said capture zone comprising receptors immobilized to said surface or immobilized on particles immobilized to said surface." Claim 79 further limits claim 74 by stating "one or more of said discrete capture zones comprise one or more particles immobilized to said surface, wherein said receptors are immobilized on said particles." The reference to "said receptors," claim 79 clearly relates to the receptors recited in claim 74, further providing that those receptors are immobilized on "particles immobilized to said surface." The Examiner's belief that these particles might not be "the alternative particles" referred to in claim 74 (Office Action, page 4) is plainly in error, as claim 74 indicates that the receptors being referred to are either on "said surface" or "on particles immobilized to said surface." Claim 79 unambiguously refers to the latter case.

In view of the foregoing, Appellant respectfully submits that the claims meet the definiteness standard, and requests that the rejection of claims 74-81 and 92-99 be withdrawn or reversed.

4. Rejection of claims 74 and 92 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under 35 U.S.C. § 102(b) for claims 74 and 92 based on Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims. For these reasons, Appellant respectfully requests that the rejection of claims 74 and 92 be withdrawn or reversed.

The Examiner's reasons for the rejection are not precisely clear. In the body of the rejection, the Examiner appears to be arguing that the claims encompass a nonporous textured surface with receptor immobilized on particles immobilized to the surface, and that "support 1(a)" of the '543 patent is equivalent to the particles of the present claims:

> Stocker teaches a device for immunological testing **of immobilized samples**. Figure 6(a) a plate (2) comprising supports (1a) within a hydrophilic area (3) for sample capture and a surrounding hydrophobic area (4). This has been read on the claimed hydrophilic/capture zones. Support 1(a) has been read on the claimed particles **that immobilize the sample**. Column 5 lines 59+ and claim 8 teach that the surface is not flat and has "depressions" where the sample can be trapped. This has been read on the claimed "textured surface."

Office Action, page 5, emphasis added.

It is clear from this passage of the rejection that the plain language of the claims has not been properly considered, and that, for this reason, the teachings of the '543 patent have not been properly applied to the rejected claims. The Examiner's conclusion that "support 1(a)" of the '543 patent "has been read on the claimed particles that immobilize the sample" is irrelevant to claims 74 and 92 because nowhere do the rejected claims refer to "particles that immobilize the sample." The devices of the present claims comprise immobilized receptors that bind target ligands from a sample. Moreover, the rejected claims provide that particles used to immobilize such receptors be in a size range of from 1 nm to 5 μm. Even the shortest dimension of the "support 1(a)" in the '543 patent is at least 40 times larger than the largest dimension recited in the claims; and the largest dimension is 400 times larger. As discussed in column 7, lines 37-39 and 49-51 of the '543 patent, the supports are made from glass "cover slips," which are used so that a tissue sample may be emplaced on a large support, and the support then divided into smaller fragments, the smallest fragment dimension being 200 μm, the largest being 2 mm.

In view of the foregoing, it appears that the Examiner attempts to shift the reasoning on which the rejection is based. In particular, on page 7 of the Office Action, the Examiner now states that "the alternative embodiment of the particles having the dimension of between 1 nm and 5 microns is not addressed in the rejections of record. The Office has correctly interpreted the instant claim language as the scenario of a nonporous smooth surface with a receptor immobilized to the surface."

If this is the case, it appears the reference is of no relevance in the rejection to "support 1(a)" reading on "the claimed particles" and "the surface" reading on the "textured surface". In addition, what is the relevance of the rejection under 35 U.S.C § 103, in which the Examiner

combines the '543 patent with a secondary reference because "Stocker is silent to the claimed material of the particles"? Office Action, page 5, last sentence. Appellant respectfully submits that the grounds of rejection are disjointed and fail to support the rejection.

To the extent that the rejection is based on "the scenario of a nonporous smooth surface with a receptor immobilized to the surface," it is again clear that the plain language of the claims has not been properly considered, and that, for this reason, the teachings of the '543 patent have not been properly applied to the rejected claims. The rejected claims refer to a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on that surface. The claims also specify that each capture zone comprises receptor immobilized to said surface *or* immobilized on particles immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands. Furthermore, the capture zones occupy one or more discrete hydrophilic regions of said surface, and are delimited by an adjacent hydrophobic region of said surface.

As the Examiner correctly notes with reference to Figure 6(a), the '543 patent discloses a "plate 2" that might correspond to the nonporous smooth or nonporous textured surface referred to in the rejected claims. This plate has a plurality of "hydrophilic reaction fields 3 and hydrophobic surrounding area 4" ('543 patent, column 5, lines 10-13) that might correspond to the "plurality of discrete capture zones on said surface" referred to in the rejected claims. But nothing in the '543 patent discloses immobilizing any receptor to those "reaction fields," or indeed to any other surface of "plate 2." To the extent the '563 patent discloses immobilizing biological materials, it is to the surface of "support 1(a)." As such, the '543 patent does not teach the first option in the claims for immobilizing a receptor -- in which receptor is immobilized on the non-porous smooth or non-porous textured surface itself. And as noted above, each "support 1(a)" in the '543 patent is 400 times larger in its largest dimension than the particle size range recited in the rejected claims. As such, the '543 patent does not teach the second option in the claims for immobilizing a receptor – in which receptor is immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to the non-porous smooth or non-porous textured surface.

The Examiner has the initial burden of establishing a *prima facie* case of anticipation by pointing out where all of the claim limitations appear in a single reference. *See, In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990); *In re King*, 801 F.2d 1324, 1327, 231 USPQ 136, 138-39 (Fed. Cir. 1986). Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 74 and 92 be withdrawn or reversed.

5. Rejection of claims 75 and 93 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under under 35 U.S.C. § 102(b) for claims 75 and 93 based on Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims.

The rejected claims depend from claims 74 and 92, and so refer to a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on that surface; each capture zone comprises receptor immobilized to said surface *or* immobilized on particles immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands; and the capture zones occupy one or more discrete hydrophilic regions of said surface, and are delimited by an adjacent hydrophobic region of said surface. As discussed in detail above, the '543 patent does not teach the first option in the claims for immobilizing a receptor -- in which receptor is immobilized on the non-porous smooth or non-porous textured surface itself; or the second option in the claims for immobilizing a receptor – in which receptor is immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to the non-porous smooth or non-porous textured surface. For this reason alone, no *prima facie* case of anticipation has been established.

Claims 75 and 93 further limit their respective independent claim, in that claims 75 and 93 specify that each capture zone comprises receptors independently selected from the group consisting of antibodies, antibody fragments, nucleic acid molecules, and chelators. Nothing in

the Examiner's statement of rejection indicates where such a teaching may be found in the '543 patent. Instead, the Examiner merely states "Stocker teaches antibodies, etc." Office Action, page 8, first complete sentence.

The Examiner's previous response to Appellant's request for additional clarity on where this claim limitation might be found in the '543 patent is instructive, in that it again reinforces the fact that the Examiner continues to apply the '543 patent to language that does not exist in the rejected claims. The Examiner has referred to column 10, lines 1-30, of the '543 patent for an alleged teaching of "antibodies to bind the ligands of interest." Office Action mailed August 31, 2006, page 4, second full paragraph. The cited portion of the '543 patent, however, is unavailing because it refers to detecting soluble antibodies in a serum sample by binding to an immobilized tissue section, and not to antibodies immobilized in a device that are capable of binding a ligand of interest. The antibodies in the '543 patent differ from the antibodies recited in the rejected claims, as the antibodies of the '543 patent are not capable of binding one or more of a plurality of target ligands. Instead, the antibodies of the '543 patent are the target ligands. Appellant respectfully submits that the particular antibodies recited in the present claims are structural elements of the claimed devices that must be considered, as it is antibody structure that drives antibody binding.

Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 75 and 93 be withdrawn or reversed.

6. Rejection of claims 76 and 94 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under 35 U.S.C. § 102(b) for claims 76 and 94 based on Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims.

The rejected claims depend from claims 74 and 92, and so refer to a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on that surface; each capture zone comprises receptor immobilized to said surface *or* immobilized on particles immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands; and the capture zones occupy one or more discrete hydrophilic regions of said surface, and are delimited by an adjacent hydrophobic region of said surface. As discussed in detail above, the '543 patent does not teach the first option in the claims for immobilizing a receptor -- in which receptor is immobilized on the non-porous smooth or non-porous textured surface itself; or the second option in the claims for immobilizing a receptor – in which receptor is immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to the non-porous smooth or non-porous textured surface. For this reason alone, no *prima facie* case of anticipation has been established.

Claims 76 and 94 further limit their respective independent claim by specifying that each capture zone binds a different target ligand from amongst the plurality of target ligands being detected. The Examiner argues that "Stocker teach in column 3 lines 27+ the use of different tissue samples in different wells which has been properly read on the claimed 'different target ligands.'" Office Action, page 8, first full paragraph. The section of the '543 patent to which the Examiner refers, however, has nothing to do with the devices disclioded in the '543 patent, or indeed with the subject matter of claims 76 and 94. Rather, this section from the "Background of the Invention" portion of the '543 patent refers to the production of compound frozen tissue sections. It says nothing about providing a device having a plurality of discrete capture zones in which each discrete capture zone binds a different target ligand from amongst a plurality of target ligands.

Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 76 and 94 be withdrawn or reversed.

7. Rejection of claims 77 and 95 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under 35 U.S.C. § 102(b) for claims 77 and 95 based on Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims.

Claims 77 and 95 also depend from claims 76 and 94, and thus require that each capture zone binds a different target ligand from amongst the plurality of target ligands being detected, a feature which is also not provided in the '543 patent.

Claims 77 and 95 further provide that the target ligands are nucleic acids, and that each capture zone comprises a nucleic acid molecule complementary to one of these target ligands. Nothing in the Examiner's statement of rejection indicates where such a teaching may be found in the '543 patent. Because the Examiner has the initial burden of establishing a *prima facie* case of anticipation by pointing out where all of the claim limitations appear in a single reference, the Examiner's failure to address the limitations of claims 77 and 95 cannot establish a *prima facie* case of anticipation of that claim.

Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 77 and 95 be withdrawn or reversed.

8. Rejection of claims 78 and 96 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under 35 U.S.C. § 102(b) for claims 78 and 96 as allegedly being anticipated by Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims.

The rejected claims depend from claims 74 and 92, and so refer to a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on

that surface; each capture zone comprises receptor immobilized to said surface *or* immobilized on particles immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands; and the capture zones occupy one or more discrete hydrophilic regions of said surface, and are delimited by an adjacent hydrophobic region of said surface. As discussed in detail above, the '543 patent does not teach the first option in the claims for immobilizing a receptor -- in which receptor is immobilized on the non-porous smooth or non-porous textured surface itself; or the second option in the claims for immobilizing a receptor – in which receptor is immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to the non-porous smooth or non-porous textured surface. For this reason alone, no *prima facie* case of anticipation has been established.

Claims 78 and 96 also depend from claims 76 and 94, and thus require that each capture zone binds a different target ligand from amongst the plurality of target ligands being detected, a feature which is also not provided in the '543 patent.

Claims 78 and 96 further provide that each capture zone comprises an antibody or antibody fragment that binds to one of these target ligands. As noted above, the Examiner merely states "Stocker teaches antibodies, etc." Office Action, page 8, first complete sentence.

The Examiner has referred to column 10, lines 1-30, of the '543 patent for an alleged teaching of "antibodies to bind the ligands of interest." Office Action mailed August 31, 2006, page 4, second full paragraph. The cited portion of the '543 patent, however, is unavailing because it refers to detecting soluble antibodies in a serum sample by binding to an immobilized tissue section, and not to antibodies immobilized in a device that are capable of binding a ligand of interest. The antibodies in the '543 patent differ from the antibodies recited in the rejected claims, as the antibodies of the '543 patent are not capable of binding one or more of a plurality of target ligands. Instead, the antibodies of the '543 patent are the target ligands. Appellant respectfully submits that the particular antibodies recited in the present claims are structural elements of the claimed devices that must be considered, as it is antibody structure that drives antibody binding.

Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 78 and 96 be withdrawn or reversed.

9. Rejection of claims 79 and 97 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under 35 U.S.C. § 102(b) for claims 79 and 97 as allegedly being anticipated by Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims.

The rejected claims depend from claims 74 and 92, and so refer to a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on that surface; each capture zone comprises receptor immobilized to said surface *or* immobilized on particles immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands; and the capture zones occupy one or more discrete hydrophilic regions of said surface, and are delimited by an adjacent hydrophobic region of said surface. As discussed in detail above, the '543 patent does not teach the first option in the claims for immobilizing a receptor -- in which receptor is immobilized on the non-porous smooth or non-porous textured surface itself; or the second option in the claims for immobilizing a receptor – in which receptor is immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to the non-porous smooth or non-porous textured surface. For this reason alone, no *prima facie* case of anticipation has been established.

Referring to terms used in the foregoing discussion of independent claims 74 and 92, claims 79 and 97 each further limit their respective independent claim by specifying that one or more of the capture zones rely on the second option for immobilizing receptor -- that in which receptor is attached to a separate solid phase, specifically a particle having the dimensions of between 1 nm and 5 μm, and the particles are themselves immobilized on the nonporous surface. As noted above, the "support 1(a)" in the '543 patent (which the Examiner reads on the particles

in the rejected claims) are 400 times larger in their the largest dimension than the particle size range recited in the claims. As discussed in column 7, lines 37-39 and 49-51, the supports in the '543 patent are made from glass "cover slips," which are used so that a tissue sample may be emplaced on a large support, and the support then divided into smaller fragments, the smallest being 200 μm, the largest being 2 mm.

Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 79 and 97 be withdrawn or reversed.

10. Rejection of claims 80 and 98 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under 35 U.S.C. § 102(b) for claims 80 and 98 as allegedly being anticipated by Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims.

The rejected claims depend from claims 74 and 92, and so refer to a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on that surface; each capture zone comprises receptor immobilized to said surface *or* immobilized on particles immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands; and the capture zones occupy one or more discrete hydrophilic regions of said surface, and are delimited by an adjacent hydrophobic region of said surface. As discussed in detail above, the '543 patent does not teach the first option in the claims for immobilizing a receptor -- in which receptor is immobilized on the non-porous smooth or non-porous textured surface itself; or the second option in the claims for immobilizing a receptor – in which receptor is immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to the non-porous smooth or non-porous textured surface. For this reason alone, no *prima facie* case of anticipation has been established.

Claims 80 and 98 also depend from claims 79 and 97, and thus require that one or more of the capture zones rely on the second option for immobilizing receptor -- that in which receptor is attached to a separate solid phase, specifically a particle having the dimensions of between 1 nm and 5 μm, and the particles are themselves immobilized on the nonporous surface. This feature is also not provided in the '543 patent.

Claims 80 and 98 further provide that the receptors attached to the particles are antibodies or antibody fragments. As noted above, the Examiner merely states "Stocker teaches antibodies, etc." Office Action, page 8, first complete sentence.

The Examiner has referred to column 10, lines 1-30, of the '543 patent for an alleged teaching of "antibodies to bind the ligands of interest." Office Action mailed August 31, 2006, page 4, second full paragraph. The cited portion of the '543 patent, however, is unavailing because it refers to detecting soluble antibodies in a serum sample by binding to an immobilized tissue section, and not to antibodies immobilized in a device that are capable of binding a ligand of interest. The antibodies in the '543 patent differ from the antibodies recited in the rejected claims, as the antibodies of the '543 patent are not capable of binding one or more of a plurality of target ligands. Instead, the antibodies of the '543 patent are the target ligands. Appellant respectfully submits that the particular antibodies recited in the present claims are structural elements of the claimed devices that must be considered, as it is antibody structure that drives antibody binding.

Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 78 and 96 be withdrawn or reversed.

11. Rejection of claims 81 and 99 under 35 U.S.C. §102(b)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of anticipation under 35 U.S.C. § 102(b) for claims 81 and 99 as allegedly being anticipated by Stöcker, U.S. Patent 4,647,543. The Examiner's recitation of features from the '543 patent does not properly address the claimed elements. Moreover, when the claimed elements are

properly addressed, it is clear that the '543 patent does not provide each and every element set forth in the claims.

The rejected claims depend from claims 74 and 92, and so refer to a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on that surface; each capture zone comprises receptor immobilized to said surface *or* immobilized on particles immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands; and the capture zones occupy one or more discrete hydrophilic regions of said surface, and are delimited by an adjacent hydrophobic region of said surface. As discussed in detail above, the '543 patent does not teach the first option in the claims for immobilizing a receptor -- in which receptor is immobilized on the non-porous smooth or non-porous textured surface itself; or the second option in the claims for immobilizing a receptor – in which receptor is immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to the non-porous smooth or non-porous textured surface. For this reason alone, no *prima facie* case of anticipation has been established.

Claims 80 and 98 also depend from claims 79 and 97, and thus require that one or more of the capture zones rely on the second option for immobilizing receptor -- that in which receptor is attached to a separate solid phase, specifically a particle having the dimensions of between 1 nm and 5 μm, and the particles are themselves immobilized on the nonporous surface. This feature is also not disclosed in the '543 patent.

Claims 80 and 98 further provide that the nonporous surface is a textured surface, and one or more of the particles are entrapped within depressions and/or between protrusions on the textured surface. Nothing in the Examiner's statement of rejection indicates where such a teaching may be found in the '543 patent. Because the Examiner has the initial burden of establishing a *prima facie* case of anticipation by pointing out where all of the claim limitations appear in a single reference, the Examiner's failure to address the limitations of claims 81 and 99 cannot establish a *prima facie* case of anticipation of the claims.

Because the '543 patent does not disclose each and every limitation of the claimed invention, no *prima facie* case of anticipation has been established. In view of the foregoing, Appellant respectfully requests that the rejection of claims 78 and 96 be withdrawn or reversed.

12. Rejection of claims 82 and 100 under 35 U.S.C. §103(a)

Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a) for claims 82 and 100 over the '543 patent, either alone or in view of either Anawis and Lindberg, U.S. Patent 5,091,318, or Rohr, U.S. Patent 5,445,970.

A. The primary '543 patent does not teach or suggest the claimed use of receptors immobilized on particles

Claim 82 depends from claim 79, which in turn depends from claim 74. Similarly, claim 100 depends from claim 97, which in turn depends from claim 92. Thus, claims 82 and 100 contain all of the limitations of these claims from which the depend, and add the additional limitation that the particles on which receptor is immobilized, and which are themselves immobilized on the nonporous surface, are selected from the group consisting of latex particles, silica particles, zirconia particles, alumina particles, titania particles, ceria particles, metal sol particles, and polystyrene particles.

The Examiner has taken the position that the only deficiency between the '543 patent and independent claims 82 and 100 are the specific materials from which the particles are made, and has asserted that the claims are obvious over the '543 alone, or in combination with either of two secondary references. Office Action, page 5, last sentence. As Appellant has discussed in detail above with regard to the anticipation rejection of claims 74 and 92, the Examiner's position in this regard is both impossibly confused and incorrect.

According to page 7 of the Office Action, "the alternative embodiment of the particles having the dimension of between 1 nm and 5 microns is not addressed in the rejections of record. The Office has correctly interpreted the instant claim language as the scenario of a nonporous smooth surface with a receptor immobilized to the surface."

If this is the case, then the Examiner concedes that the rejection is not based on assertion that the primary '543 patent includes the invention recited in the rejected claims -- a device having a nonporous smooth or nonporous textured surface, and a plurality of discrete capture zones on that surface; where one or more capture zone comprises receptor immobilized on particles in a size range from 1 nm to 5 μm, which particles are immobilized to said surface, the receptor being capable of binding one or more of said plurality of target ligands; and where the capture zones occupy one or more discrete hydrophilic regions of said surface delimited by an adjacent hydrophobic region of said surface.

Further, if this is the case, then simply adding a secondary reference disclosing certain materials out of which particles might be made does not establish a *prima facie* case of obvious, as the Examiner's analysis is not based on the use of particles in the primary reference. The failure of the Examiner to appreciate this fact is further evidence that the rejection is so confused that the Examiner himself does not understand the basis on which the claims are rejected.

B. The Examiner has not articulated any reasoning for the artisan to either modify the '543 patent, or to combine the cited art, to arrive at the claimed invention

The noted deficiencies in the '543 patent cannot be cured without additional teachings, which are notably lacking from this obviousness rejection. Rejections on obviousness grounds must be based on some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness of the claimed invention. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988, 78 U.S.P.Q.2d 1329, 1336 (Fed. Cir. 2006)). Because the Examiner incorrectly presumes that the '543 patent anticipates the claims from which claims 82 and 100 depend, no such reasoning is provided by the Examiner to modify the teachings of the '543 patent in order to actually arrive at the invention claimed in claims 82 and 100, or to combine the '543 patent with the secondary references.

As far as the Examiner's remarks concerning the additional limitations contained in the rejected claims, the Examiner relies on an assertion that the '543 patent "is silent to the material construction of particles," and that the sort of materials recited in claims 82 and 100 are "well known for their inertness, availability, and long track record of use with immunological

materials." Office Action, page 6. But the '543 patent is not silent on the composition of the supports used to immobilize tissue samples, as the Examiner asserts.

In fact, in all cases, the supports in the '543 patent are made of thin glass.

Glass "cover slip" material is selected for use in the '543 patent so that a tissue sample may be emplaced on a large support, and the support then divided into smaller fragments by breaking or cutting, such that each resulting glass fragment contains some of the same tissue sample. *See, e.g.*, '543 patent, column 7, lines 33-66; Examples 1 and 2; and claims. The smallest dimension of these glass fragments is about 200 μm; and the largest is 2 mm. '543 patent, column 7, line 50. Nothing of record indicates that materials such as latex, zirconia, alumina, and titanium, whatever their "long track record" for other uses, could be processed in the manner that the glass supports disclosed in the '543 patent are processed without destroying the specimen emplaced thereon, or that latex, zirconia, alumina, and titanium might be "easily dividable" ('543 patent, column 7, line 57) in the manner of a glass cover slip. Moreover, the primary '543 patent is directed to preparing immunohistochemical samples to be viewed by light microscopy. How latex, zirconia, alumina, and titanium surfaces could be used in place of glass for light microscopy is not discussed by the Examiner.

The Examiner also avers that "the Office would maintain the selection of the claimed [particle] size would have been obvious as a result effective variable." Office Action, page 8. While discovery of an optimum value of a variable in a known process may be obvious, an exception to this general rule exists where the parameter optimized was not recognized to be a result effective variable. *In re Antonie*, 559 F.2d 618, 621, 195 USPQ 6, 8 (CCPA 1977). It is unclear, and the Examiner does not explain, why the artisan would have considered reducing the size of such particles 400-fold "a variable which achieves a recognized result" (MPEP § 2144.05 (II)(B)). Indeed, how support fragments 400-fold smaller than those recited in the '543 patent could even be effectively produced and used according to the methods of the '543 patent is unclear. In the present case, the primary '543 patent prepares an immunohistochemical sample by adhering a tissue sample to a glass support, which support is then divided into smaller fragments, the largest dimensions of which are 400 times those of the particles in the present

claims. '543 patent, column 7, line 50. Reducing the size of the support fragments from the '543 patent would be neither appropriate nor effective in the methods for which the glass fragments are used.

Apellant respectfully submits that, without knowledge of the presently claimed invention, the skilled artisan would not utilize the materials recited in claims 82 and 100 in place of the thin glass cover slip supports disclosed in the '543 patent, as such a modification would render the resulting tissue supports unsatisfactory for their intended purpose. Additionally, the skilled artisan would not consider particle size to be a result effective variable that might be optimized by reducing the dimensions of the glass cover slip fragments to the dimensions recited in the present claims.

C. *No* prima facie *case of obviousness has been established*

The Examiner bears the initial burden of establishing a *prima facie* case of obviousness. In the present case, the Examiner has not met that burden. The '543 patent does not teach or suggest each and every element of the present claims, and no reasoning with some rational underpinning has been articulated for the skilled artisan to modify the '543 patent, alone or in combination with the cited secondary references, to provide each of the elements of the present claims. In view of the foregoing, Appellant respectfully requests that the rejection of claims 82 and 100 under 35 U.S.C. § 103(a) be withdrawn or reversed.

Conclusion

For the reasons discussed above, Appellant respectfully submits that claims 74-84 and 92-100 are in condition for allowance, and respectfully request that the rejections be withdrawn or reversed, and that the claims be allowed to issue.

Fee Authorization

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. **23-2415** (Docket No. 36671-716.505).

Respectfully submitted,

Date: March 10, 2003

By: _____

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Appendix A: Text of the Claims Involved in the Appeal

74. An assay device for detecting a plurality of target ligands in a sample, comprising:

a nonporous smooth surface or a nonporous textured surface, said nonporous textured surface comprising one or more depressions or protrusions extending between 1 nm and 0.5 mm from said nonporous textured surface; and

a plurality of discrete capture zones on said surface, each said capture zone comprising receptors immobilized to said surface or immobilized on particles immobilized to said surface, wherein said particle size range is from 1 nm to 5 μm, and wherein said receptors are capable of binding one or more of said plurality of target ligands,

wherein said capture zones occupy one or more discrete hydrophilic regions of said surface delimited by an adjacent hydrophobic region of said surface.

75. An assay device according to claim 74, wherein each said discrete capture zone comprises receptors independently selected from the group consisting of antibodies, antibody fragments, nucleic acid molecules, and chelators.

76. An assay device according to claim 74, wherein each said discrete capture zone binds a different target ligand from amongst said plurality of target ligands.

77. An assay device according to claim 76, wherein said plurality of target ligands are a plurality of nucleic acid molecules, and each said discrete capture zone comprises a nucleic acid molecule having a nucleotide sequence that is complementary to one of said plurality of nucleic acid molecules.

78. An assay device according to claim 76, wherein each said discrete capture zone comprises an antibody, or a fragment thereof, capable of binding one of said plurality of target ligands.

79. An assay device according to claim 74, wherein one or more of said discrete capture zones comprise one or more particles immobilized to said surface, wherein said receptors are immobilized on said particles.

80. An assay device according to claim 79, wherein said receptors are antibodies, or fragments thereof.

81. An assay device according to claim 79, wherein said surface is said textured surface, and one or more of said particles are entrapped within depressions and/or between protrusions on the textured surface.

82. An assay device according to claim 79, wherein said particles are selected from the group consisting of latex particles, silica particles, zirconia particles, alumina particles, titania particles, ceria particles, metal sol particles, and polystyrene particles.

83. An assay device according to any one of claims 74-82 and 92-100, wherein said nonporous surface forms a capillary space between said nonporous surface and a second surface spaced at a capillary forming distance from said nonporous surface.

84. An assay device according to any one of claims 74-82 and 92-100, wherein said nonporous surface is not part of a capillary space.

85-91. Cancelled.

92. An assay device for detecting a plurality of target ligands in a sample, comprising:

a nonporous smooth surface or a nonporous textured surface, said nonporous textured surface comprising one or more depressions or protrusions extending between 1 nm and 0.5 mm from said nonporous textured surface; and

a plurality of discrete capture zones on said surface, each said capture zone comprising receptors immobilized thereon to said surface or immobilized on particles immobilized to said surface, wherein said particle size range is from 1 nm to 5 μm, and wherein said receptors are capable of binding one or more of said plurality of target ligands,

wherein said capture zones are located in one more diagnostic elements of said surface, said diagnostic elements being hydrophilic and delimited by one or more adjacent hydrophobic regions of said surface.

93. An assay device according to claim 92, wherein each said discrete capture zone comprises receptors independently selected from the group consisting of antibodies, antibody fragments, nucleic acid molecules, and chelators.

94. An assay device according to claim 92, wherein each said discrete capture zone binds a different target ligand from amongst said plurality of target ligands.

95. An assay device according to claim 94, wherein said plurality of target ligands are a plurality of nucleic acid molecules, and each said discrete capture zone comprises a nucleic acid molecule having a nucleotide sequence that is complementary to one of said plurality of nucleic acid molecules.

96. An assay device according to claim 94, wherein each said discrete capture zone comprises an antibody, or a fragment thereof, capable of binding one of said plurality of target ligands.

97. An assay device according to claim 92, wherein one or more of said discrete capture zones comprise one or more particles immobilized to said surface, wherein said receptors are immobilized on said particles.

98. An assay device according to claim 97, wherein said receptors are antibodies, or fragments thereof.

99. An assay device according to claim 97, wherein said surface is said textured surface, and one or more of said particles are entrapped within depressions and/or between protrusions on the textured surface.

100. An assay device according to claim 97, wherein said particles are selected from the group consisting of latex particles, silica particles, zirconia particles, alumina particles, titania particles, ceria particles, metal sol particles, and polystyrene particles.

Appendix B: Evidence Appendix

Appendix C: Related Appeals and Interferences

U.S. Patent Application 10/153,423;

U.S. Patent Application 10/697,351.